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EXAMINER
ALLEN, M

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 12/2/92 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1, 10, 12-15, 6-9 are pending in the application.
   Of the above, claims 6-9 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1, 10, 12-15 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Claims 1, 6-10, and 12-15 have been canceled. Applicant has added claims 1-15 which have been renumbered as claims 16-30, respectively, in accordance with 37 C.F.R. 1.126. Applicant is reminded to number claims appropriately if any additional claims are introduced.

Applicant's arguments filed 25 March 1994 have been fully considered but they are not deemed to be persuasive or are deemed moot in view of the new grounds of rejection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 18, 21-22, 29 are objected to as failing to include the formula for formula I. A claim should be self-contained and not require reference to the specification.

Claim 17 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 17 of U.S. Patent No. 5,227,293.

This rejection is maintained for reasons of record as applied to claim 6 in the prior Office action.

Applicant argues that methods of the two claims are patentably distinct because the method of patent '293 does not include a step of cleaving the fusion protein. This difference was acknowledged in the rejection and the reasons why inclusion of this step was obvious set forth. It is maintaned that this is a routine step when using fusion protein techniques as evidenced by at least Markussen et al. (U.S. Patent No. 4,916,212) at column 3, line 52, through column 4, line 40, and Goeddel et al. (EPO 055,945) as set forth in the prior Office action. It is further noted that the method of the instant claim does not specify the ballast constituent.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed.

The claims have been amended to include limitations to incubating the compound of formula I with trypsin under slightly acidic conditions at a pH of about 6.8 where phenol and other similar aromatics are not present. The basis in the specification for these limitations is not clear and has not been pointed out. Page 21 of the response references page 15, lines 24-26; however, this does not provide basis for the above limitations.

Claims 21-23, 25-27, 29-30 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 17, 21-23, 28-29 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to production in bacteria as fusion proteins. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The specification does not describe nor enable production of

insulin precursors in E. coli except as fusion proteins. It would have been well known that small peptides such as insulin precursors were prone to degradation when not produced as fusion proteins. These claims encompasses non-fusion proteins being produced in E. coli.

Claims 17 and 28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is confusing because it implies that formula I represents more than one compound in reciting "if the gene structure also encodes for a fusion protein." It appears that formula I represents a single compound rather than several compounds.

Claim 28 is confusing because it implies that formula I represents more than one compound in reciting "compound of formula I is part of a fusion protein." It appears that formula I represents a single compound rather than several compounds.

It is suggested that the claims clearly reflect whether a fusion protein is present or not. Conditional steps tend to be confusing and unclear.

Claims 16 and 18-20 are rejected under 35 U.S.C. § 103 as

being unpatentable over either Markussen et al. (U.S. Patent No. 4,916,212) or Markussen et al. (EPO 163,529)

This rejection is maintained for reasons of record as applied to claims 1 and 6-9 in the prior Office action.

It is noted that claim 20 is limited to a bacterium rather than any host cell. However, Markussen et al. discloses E. coli holding plasmids encoding the desired insulin precursors and this claim is still deemed to be obvious.

It is maintained that both Markussen et al. references suggest the claimed compound of formula I. It is maintained that one would have had a high expectation of success in producing the claimed insulin precursor.

Claims 17, 20, and 28 are rejected under 35 U.S.C. § 103 as being unpatentable over Markussen et al. (EPO 163,529) or Markussen et al. (U.S. Patent No. 4,916,212) either in view of Goeddel et al. (EPO 055,945).

This rejection is maintained for reasons of record as applied to claim 6 in the prior Office action. The Markussen et al. 4,946,828 patent was cited in the prior ground of rejection; however, it was clear from the context of the rejection that this was a typographical error and that the Markussen et al. 4,916,212 patent was intended. It is noted that the method claims have been limited to production in bacteria. Goeddel et al. teaches production in E. coli.

Claim 24 is rejected under 35 U.S.C. § 103 as being unpatentable over Markussen et al. (EPO 163,529) or Markussen et al. (U.S. Patent No. 4,916,212) either in view of Goeddel et al. (EPO 055,945) and Mai et al. (U.S. Patent No. 5,087,564).

This rejection is maintained for reasons of record as applied to claim 10 in the prior Office action. The Markussen et al. 4,946,828 patent was cited in the prior ground of rejection; however, it was clear from the context of the rejection that this was a typographical error and that the Markussen et al. 4,916,212 patent was intended.

The bridging sequence has not been shown to be critical to the invention and one of ordinary skill in the art would have routinely employed known cleavage sequences for their known and useful purposes in producing fusion proteins.

With respect to the above art rejections concerning fusion proteins it is noted that E. coli has long been used to produce desirable precursors to insulin and that fusion proteins are often used for small peptides. It is maintained that it would have been obvious to produce the insulin precursor of Markussen et al. in E. coli as taught by the modifying references. The fact that Markussen et al. chose to produce the precursor in yeast does not teach away. Given the extensive teachings in the prior art of record of producing insulin precursors in E. coli there would have

been a high expectation of success.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen, whose telephone number is (703) 308-0666. The examiner can normally be reached on Monday-Thursday from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Garnette D. Draper, can be reached on (703) 308-4232. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

GARNETTE D. DRAPER
SUPERVISORY PATENT EXAMINER
GROUP 1800